Clinical Policy Title:	CNS stimulants
Policy Number:	RxA.089
Drug(s) Applied:	Focalin XR®, Adhansia XR®, Aptensio XR®, Jornay PM®, Daytrana®, Quillichew ER®, Quillivant XR®, Cotempla XR-ODT®, Mydayis®, Adzenys ER™, Dyanavel XR®, Adzenys XR-ODT™
Original Policy Date:	02/07/2020
Last Review Date:	01/17/2023
Line of Business Policy Applies to:	All lines of business

Background

The following are the central nervous system (CNS) stimulants requiring prior authorization:

- amphetamine extended-release orally disintegrating tablets (Adzenys XR-ODT™)
- amphetamine extended-release oral suspension (Adzenys ER™, Dyanavel XR®)
- mixed salts of a single entity amphetamine product extended-release (Mydayis®)
- dexmethylphenidate extended-release (Focalin XR®)
- methylphenidate extended-release (Adhansia XR®, Aptensio XR™, Jornay PM®)
- methylphenidate transdermal system (Daytrana®)
- methylphenidate extended-release chewable tablets (Quillichew ER®)
- methylphenidate extended-release oral suspension (Quillivant XR®)
- methylphenidate extended-release orally disintegrating tablets (Cotempla XR-ODT®)

Extended-release methylphenidate and amphetamine products are indicated for attention deficit/hyperactivity disorder (ADHD).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
amphetamine ER oral suspension (Adzenys ER™)	ADHD	Patients 6 to 17 years: 6.3 mg (5 mL) orally once daily Adults: 12.5 mg (10 mL) orally once daily	6 to 12 years: 18.8 mg (15 mL)/day 13 years and older: 12.5 mg (10 mL)/day
amphetamine ER orally disintegrating tablet (Adzenys XR-ODT™)		Patients 6 to 17 years: 6.3 mg orally once daily Adults: 12.5 mg orally once daily	6 to 12 years: 18.8 mg/day 13 years and older: 12.5 mg/day
methylphenidate ER (Adhansia XR®)		Patients 6 years of age and older: Starting dose 25 mg orally once daily, dose may be increased in increments of 10 to 15 mg at intervals of at least 5 days.	Pediatrics: 70 mg/day Adults: 85 mg/day

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
methylphenidate ER (Aptensio XR®)	ADHD	Patients 6 years of age and older: Starting dose 10 mg orally once daily, dose may be increased weekly in increments of 10 mg per day.	60 mg/day
methylphenidate ER (Jornay PM®)		Patients 6 years of age and older: Starting dose 20 mg orally at bedtime, dose may be increased weekly in increments of 20 mg per day.	100 mg/day
methylphenidate ER orally disintegrating tablet (Cotempla XR-ODT®)		Patients 6 to 17 years: Starting dose 17.3 mg orally once daily day, dose may be increased weekly in increments of 8.6 mg to 17.3 mg per day.	51.8 mg/day
dexmethylphenidate ER (Focalin XR®)		Pediatric patients: Starting dose 5 mg orally once daily, dose may be increased weekly in increments of 5 mg per day. Adult patients: Starting dose 10 mg orally once daily, dose may be increased weekly in increments of 10 mg per day.	Pediatrics: 30 mg per day Adults: 40 mg per day
methylphenidate transdermal system (Daytrana®)		10 mg applied to the hip area (using alternating sites) 2 hours before an effect is needed and should be removed 9 hours after application	30 mg/9-hour patch per day
amphetamine oral suspension/tablet (Dyanavel XR®)		Patients 6 years and older: Starting dose 2.5 or 5 mg orally once daily in morning, dose may be increased in increments of 2.5 mg to 10 mg per day every 4 to 7 days	20 mg/day
mixed salts of a single-entity amphetamine product extended release (Mydayis®)		Patients 13 years and older: Starting dose 12.5 mg orally once daily, dose may be increased in increments of 12.5 mg no sooner than weekly. Adult patients with severe renal impairment: 25 mg; Use in adult patients with ESRD is not recommended Pediatric patients with severe renal impairment: 12.5 mg; Use in pediatric patients with ESRD is not recommended.	Paediatrics (13 to 17 years): 25 mg/day Adults: 50 mg/day
methylphenidate chewable tablet (Quillichew ER®)		Patients 6 years and older: Starting dose 20 mg orally once daily, dose may be increased weekly in increments of 10, 15 or 20 mg per day.	60 mg/day

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
methylphenidate ER oral suspension (Quillivant XR®)	ADHD	Patients 6 years and older: Starting dose 20 mg orally once daily, dose may be increased weekly in increments of 10 to 20 mg per day.	60 mg/day

Dosage Forms

- amphetamine (Adzenys ER™): Extended-release oral suspension, 1.25 mg/mL
- amphetamine (Adzenys XR-ODT™): Extended-release orally disintegrating tablets, 3.1 mg, 6.3 mg, 9.4 mg, 12.5 mg, 15.7 mg and 18.8 mg
- methylphenidate ER (Adhansia XR®): Extended-release capsules, 25 mg, 35 mg, 45 mg, 55 mg, 70 mg and 85 mg
- methylphenidate ER (Aptensio XR®): Extended-release capsules, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg and 60 mg
- methylphenidate ER (Jornay PM®): Extended-release capsules, 20 mg, 40 mg, 60 mg, 80 mg and 100 mg
- methylphenidate ER orally disintegrating tablet (Cotempla XR-ODT®): Extended-release orally disintegrating tablets, 8.6 mg, 17.3 mg and 25.9 mg
- dexmethylphenidate (Focalin XR®): Extended-release capsules, 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg and 40 mg
- methylphenidate transdermal system (Daytrana®): Transdermal patch, 10 mg/9 hours, 15 mg/9 hours, 20 mg/9 hours, and 30 mg/9 hours
- amphetamine (Dyanavel XR®): Extended-release oral suspension, 2.5 mg/mL and extended-release tablets: 5 mg (functionally scored), 10 mg, 15 mg and 20 mg
- amphetamine dextroamphetamine extended-release (Mydayis®): Extended-release capsules, 12.5 mg, 25 mg, 37.5 mg and 50 mg
- methylphenidate chewable (Quillichew ER®): Extended-release chewable tablets, 20 mg, 30 mg and 40 mg
- methylphenidate oral suspension (Quillivant XR®): Extended-release oral suspension, 25 mg/5mL (5 mg/mL)

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Attention Deficit Hyperactivity Disorder (must meet all)**:**

1. Diagnosis of ADHD;
2. Request is for Mydayis®: Age ≥ 13 years, for all other brands: Age ≥ 6 years;
3. Member meets one of the following (a or b):
   a. Trail and failure of one preferred formulary extended-release amphetamine and one preferred formulary extended-release methylphenidate at maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Request is for Adzenys ER™, Adzenys XR-ODT™, Cotempla XR-ODT®, Daytrana®, Dyanavel XR®, Quillichew ER®, or Quillivant XR® and documentation supports inability to use dosage forms available on the drug formulary (e.g., inability to swallow tablets or capsules);
4. Dose does not exceed any one of the following (a to j):

a. Adhansia XR®: 85 mg per day (adults); 70 mg/day (pediatric)
b. Adzenys ER™: 15 mL per day;
c. Adzenys XR-ODT™: 12.5- 18.8 mg per day;
d. Cotempla XR-ODT®: 51.8 mg per day;
e. Daytrana®: 30 mg per day;
f. Dyanavel XR®: 20 mg per day;
g. Focalin XR®: 30 mg per day (pediatric patients), 40 mg per day (adults);
h. Jornay PM®: 100 mg per day;
i. Mydayis®: 25 mg per day (pediatric patients), 50 mg per day (adults);
j. Quillichew ER®, Quillivant XR®, Aptensio XR®: 60 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. Attention Deficit Hyperactivity Disorder (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed any one of the following (a to j):
   a. Adhansia XR®: 85 mg per day (adults); 70 mg/day (pediatric);
   b. Adzenys ER™: 15 mL per day;
   c. Adzenys XR-ODT™: 12.5- 18.8 mg per day;
   d. Cotempla XR-ODT®: 51.8 mg per day;
   e. Daytrana®: 30 mg per day;
   f. Dyanavel XR®: 20 mg per day;
   g. Focalin XR®: 30 mg per day (pediatric patients), 40 mg per day (adults);
   h. Jornay PM®: 100 mg per day;
   i. Mydayis®: 25 mg per day (pediatric patients), 50 mg per day (adults);
   j. Quillichew ER®, Quillivant XR®, Aptensio XR™: 60 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ADHD: Attention-deficit and hyperactivity disorder
CNS: Central nervous system
FDA: Food and Drug Administration
MAO: Monoamine oxidase
SSRIs: Selective serotonin reuptake inhibitor
SNRIs**:** Serotonin and norepinephrine reuptake inhibitors

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose

methylphenidate extended release (Ritalin LA®, Concerta®)	Concerta®: 18 - 36 mg orally once daily Ritalin LA®: 20 my orally once daily	Concerta®: 72 mg/day Ritalin LA®, Metadate®: 60 mg/day
amphetamine (Adderall XR®)	Patients 6-17 years: 10 mg orally once daily Adults: 20 mg orally once daily	Patients 6 years and older: 30 mg/day Adults: 20 mg/day
dextroamphetamine (Dexedrine ER®)	5 mg orally once daily/twice daily	40 mg/day
Vyvanse®	30 mg orally once daily	70 mg/day

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):*
  - All CNS stimulants above: Hypersensitivity; use with monoamine oxidase (MAO) inhibitor, or within 14 days of last MAO inhibitor dose.
  - Daytrana®: Hypersensitivity; use with monoamine oxidase (MAO) inhibitor, or within 14 days of last MAO inhibitor dose; marked anxiety, tension, or agitation; glaucoma; tics or family history of Tourette's syndrome.

  *Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed Warning(s):
  - High potential for abuse and dependence

APPENDIX D: General Information

- Use of CNS stimulants may cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychiatric illness. Evaluate for bipolar disorder prior to Jornay PM® use.
- Sudden death has been reported in association with CNS stimulants at recommended doses in pediatric patients with structural cardiac abnormalities or other serious heart problems. In adults, sudden death, stroke, and myocardial infarction have been reported. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmias, or coronary artery disease.
- Increased risk of serotonin syndrome can occur when co-administered with serotonergic agents (e.g., SSRIs, SNRIs, triptans) but also during overdosage situations. If it occurs, discontinue Mydayis® and initiate supportive treatment.

References

1. Focalin XR® Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=1a1da905-42a0-4748-9c39-67eca45deccc&type=display. Accessed October 06, 2022.
2. Adhansia XR® Prescribing Information. Wilson, NC: Purdue Pharmaceuticals; June 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=80e15bd0-4d56-75f0-ab5a-885879fc56e9&type=display. Accessed October 06, 2022.

3. Aptensio XR® Prescribing Information. Greenville, North Carolina: Patheon Manufacturing Services LLC: June 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=5adedc01-ebf0-11e3-ac10-0800200c9a66&type=display. Accessed October 06, 2022.
4. Jornay PM® Prescribing Information. Cherry Hill, NJ: Ironshore Pharmaceuticals, Inc.; June 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=d95dede0-b1ff-4489-8f91-3bbe122852bf&type=display. Accessed October 06, 2022.
5. Daytrana® Prescribing Information. Miami, FL: Noven Therapeutics, LLC; June 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=2c312c31-3198-4775-91ab-294e0b4b9e7f&type=display. Accessed October 06, 2022.
6. Quillichew ER® Prescribing Information. Monmouth Junction, NJ: Tris Pharma; June 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=defc1205-8e90-4b1e-b862-05e4c35c7364&type=display. Accessed October 06, 2022.
7. Quillivant XR® Prescribing Information. Monmouth Junction, NJ: Tris Pharma; June 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=c2dc2109-44a6-4797-b04e-18761dd9d45a&type=display. Accessed October 06, 2022.
8. Cotempla XR-ODT® Prescribing Information. Grand Prairie, TX: Neos Therapeutics; June 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=33f70f58-c871-42c8-8adb-345caeafefcd&type=display. Accessed October 06, 2022.
9. Mydayis® Prescribing Information. Lexington, MA: Takeda Pharmaceuticals America, Inc. January 2022. Available at: http://pi.shirecontent.com/PI/PDFs/Mydayis_USA_ENG.pdf. Accessed October 07, 2022.
10. Adzenys ER™ Prescribing Information. Grand Prairie, TX: Neos Therapeutics; September 2017. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/204325s000lbl.pdf. Accessed October 06, 2022.
11. Dyanavel XR® Prescribing Information. Monmouth Junction, NJ: Tris Pharma: July 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=a8a7eb93-4192-4826-bbf1-82c06634f553&type=display. Accessed October 06, 2022.
12. Adzenys XR-ODT™ Prescribing Information. Grand Prairie, TX: Neos Therapeutics. March 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=c1179269-00b5-48ea-972d-31e614e99b7e&type=display. Accessed October 06, 2022.
13. American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with Attention-Deficit/Hyperactivity Disorder. J Am Acad Child Adolesc Psychiatry. 2007; 46(7):894-921. Available at: https://pubmed.ncbi.nlm.nih.gov/17581453/. Accessed October 06, 2022.
14. Wolraich ML, Hagan JF, Allan C, et al. Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. Pediatrics. 2019;144(4):e20192528. Available at: https://publications.aap.org/pediatrics/article/144/4/e20192528/81590/Clinical-Practice-Guideline-for-the-Diagnosis. Accessed October 07, 2022.
15. CDC. Adhd treatment recommendations | cdc. Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/ncbddd/adhd/guidelines.html. Accessed October 06, 2022.
16. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2022. Available at: http://www.clinicalkey.com. Accessed October 06, 2022.
17. Lexi-Drugs. Lexicomp. Wolters Kluwer. Hudson, Oh. Available at: https://online.lexi.com. Accessed October 06, 2022.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Updated grammar/formatting	04/2020	/2020
Policy was reviewed and updated.	01/27/2021	3/09/2021

1. Clinical policy title and lines of business updated. 2. Duration of approval for initial and continued therapy updated to 12 months. 3. Continued therapy criteria II.A.1 was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance…”. 4. References were updated.		
Policy was reviewed and updated. 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Initial Approval Criteria, I.A.2: Updated age criteria from Member age is ≥ 6 years to Request is for Mydayis® and member age is ≥ 13 years, for all other brands member age is ≥ 6 years. 3. Continued Therapy Approval Criteria II.A.3.i: Updated to include new dosing criteria Mydayis®: 25 mg per day (pediatric patients). 4. Appendix B, Vyvanse: Updated to remove unavailable generic therapeutic alternative lisdexamfetamine. 5. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 6. Appendix A: Updated to include abbreviations MAO, SSRIs and SNRIs. 7. References were reviewed and updated. 8. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C.	11/24/2021	01/17/2022
Policy was reviewed and updated. 1. Dosing Information, Dosing Regimen, mixed salts of a single-entity amphetamine product extended release (Mydayis®): Updated to include renal impairment dosing information for indication ADHD. 2. Dosage Forms: Updated to include new dosage form, extended-release tablets for drug amphetamine (Dyanavel XR®). 3. Initial Approval Criteria, I.A.4.a: Updated dosing criteria from Adhansia XR®: 85 mg per day to Adhansia XR™: 85 mg per day (adults); 70 mg/day (pediatric).	10/07/2022	01/17/2023

4. Continued Therapy Approval Crtieria, II.A.3.a: Updated dosing criteria from Adhansia XR®: 85 mg per day to Adhansia XR®: 85 mg per day (adults); 70 mg/day (pediatric). 5. Appendix B, Maximum Dose, Adderall XR®: Updated maximum dose information from Patients 6 years and older: 40 mg/day to 30 mg/day for indication ADHD and included Adults: 20 mg/day. 6. References were reviewed and updated.		